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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,947	09/22/2000	Stephen James Russell	07039-298001	9619

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	12

DATE MAILED: 09/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/667,947	Applicant(s) RUSSELL ET AL.	
	Examiner Shin-Lin Chen	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *5-19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,20 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of group I, claims 1-4, 20 and 22-26, in Paper No. 10 is acknowledged.

2. Claims 5-19 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 10.

Claims 1-26 are pending and claims 1-4, 20 and 22-26 are under consideration.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. The specification fails to provide sequence identifier for the nucleotide and amino acid sequences listed on pages 31, 46-49, 52, 59, 63 and 70-72. Each nucleotide or amino acid sequence in the specification needs to have a sequence identifier, such as SEQ ID No. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 4, 20 and 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "the method of claim 4" in claim 4 is vague and renders the claim indefinite. It is unclear what is intended to be claimed. A claim can not depend on itself.

The phrase "The method of any one of claims 1, 5, 6, 7, 9, 16, 20 or 21" in claim 22 is vague and renders the claim indefinite. Claims 5, 6, 7, 9, 16 and 21 are non-elected claims. It is unclear what is intended to be claimed in claim 22. Claims 23-26 depend on claim 22 but fails to clarify the indefiniteness.

The phrase "the kit comprising a replication-competent **Paramyxoviridae virus** comprising...d) a **Paramyxoviridae virus**" in claim 20 is vague and renders the claim indefinite. It is unclear how a virus comprises a virus.

5. Claim 22 recites the limitation "The method of any one of claims 1...20..." in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 20 is a kit claim which is a product not a method.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 20 and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-4, 20 and 22-26 are directed to a method of monitoring a reduction in tumor size in a patient comprising administering to a patient a replication-competent Paramyxoviridae virus containing a nucleic acid encoding a heterologous polypeptide and detection of said heterologous polypeptide in a biological fluid of said patient is indicative of the virus growth and reduction in tumor size in said patient, and a kit for treatment of a patient having a tumor comprising a replication-competent Paramyxoviridae virus comprising one or more of a nucleic acid encoding a heterologous polypeptide, a recombinant F, H, or M protein of said Paramyxoviridae virus, or a nucleic acid sequence encoding a cytokine. Claims 3 and 4 specify the Paramyxoviridae comprises a chimeric gene encoding a recombinant fusion protein comprising said heterologous polypeptide fused to an endogenous polypeptide and a protease cleavage site as an amino acid linker.

The specification generates Measles Virus (MV) for enhancing fusogenecity by modifying MV F, H, or M protein, recombinant MV expressing single chain antibody (ScAb) against CD38 or CEA on the surface of the virus to alter targeting specificity, and shows co-

expression of F protein with chimeric HXL (long linker arm between H protein and scAb) in MC38-CEA cells led to extensive syncytia formation.

The specification fails to provide adequate guidance and evidence for how the detection of a heterologous polypeptide in a biological fluid after administering a replication-competent Paramyxoviridae virus expressing said heterologous polypeptide to a patient would be indicative of Paramyxoviridae growth in said patient and reduction in tumor size. The specification fails to provide the correlation between the detection of a heterologous polypeptide in a biological fluid and Paramyxoviridae virus growth and reduction in tumor size in a patient. There is no evidence of record that detection of a C-peptide or cleavage product of proopiomelanocortin, preproenkephalin, preprodynorphin etc., or any peptide hormone precursors or detection of a certain level of C-peptide in a biological fluid, such as blood, urine, saliva, interstitial fluid, lymph, or cerebrospinal fluid, of a patient would be indicative of Paramyxoviridae virus growth or reduction in tumor size in said patient. Absent such correlation, one skilled in the art at the time of the invention would not know whether detection of a heterologous polypeptide in a biological fluid would be indicative of Paramyxoviridae virus growth or reduction in tumor size in a patient.

The claims encompass various administration routes of the replication-competent paramyxoviridae virus. The specification fails to provide adequate guidance and evidence whether there is any detectable heterologous polypeptide in a biological fluid when the recombinant Paramyxoviridae virus is administered intratumorally or locally into the brain in

which the virus will likely stay in the tumor or locally in the brain. There is no evidence of record that the expressed heterologous polypeptide in the recombinant Paramyxoviridae virus would be present or sufficient detectable heterologous polypeptide would be present in the biological fluid, such as blood, urine, saliva etc., and the detection of said heterologous polypeptide would be indicative of the reduction in tumor size.

The claims encompass various type of tumors at different locations of a patient. The specification fails to provide adequate guidance and evidence that detection of heterologous polypeptide in a biological fluid would be indicative of reduction of various type of tumors in size in a patient when the recombinant Paramyxoviridae virus is administered systemically. When the recombinant Paramyxoviridae virus is administered systemically, the virus will likely concentrate in liver. There is no evidence of record that detection of heterologous polypeptide in a biological fluid after administering the recombinant Paramyxoviridae virus systemically would be indicative of the reduction in tumor size of various type of tumors, such as melanoma, brain tumor, prostate cancer, testicular tumor etc.

In view of the reasons set forth above, one skilled in the art at the time of the invention would not know how to use the claimed invention and would require undue experimentation to practice over the full scope of the invention claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the absence of working examples and scarcity of guidance in the specification, and the unpredictable nature of the art.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claim 20 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kirn et al., 1996 (Molecular Medicine Today, 2(12): 519-527, IDS-AGGG).

Claim 20 is directed to a kit for treatment of a patient having a tumor comprising a replication-competent Paramyxoviridae virus comprising one or more of a nucleic acid encoding a heterologous polypeptide, a recombinant F, H, or M protein of said Paramyxoviridae virus, or a nucleic acid sequence encoding a cytokine.

Kirn teaches that replication-competent viruses are used as selective cancer therapeutics and the specific viruses used include tumor-targeting herpes simplex viruses, Newcastle disease viruses and adenoviruses. Infection of a tumor cell with a replicating virus can increase the

sensitivity of the cell to killing by cytokines such as TNF-alpha and interferon alpha. Kirn also teaches that addition of cytokine gene, such as IL-2, to replicating virus genome can increase tumor killing effect (e.g. abstract, box 2, p. 521). Thus, claim 20 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kirn et al., 1996.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Scott Priebe can be reached on (703) 308-7310. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.